

# INTERNATIONAL COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

03 JUL 2004

Applicant's or agent's file reference <b>PCA21266/HMY</b>	<div style="display: flex; justify-content: space-between;"> <div><b>FOR FURTHER ACTION</b></div> <div>See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)</div> </div>	
International application No. <b>PCT/KR02/02434</b>	International filing date (day/month/year) 26 DECEMBER 2002 (26.12.2002)	Priority date (day/month/year) 09 JANUARY 2002 (09.01.2002)
International Patent Classification (IPC) or national classification and IPC  <b>IPC7 C07D 309/06</b>		
Applicant  <b>HANMI PHARM. CO., LTD. et al</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

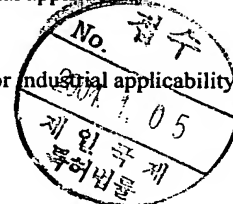
2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application



Date of submission of the demand  21 JULY 2003 (21.07.2003)	Date of completion of this report  30 DECEMBER 2003 (30.12.2003)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer  WON, Ho Joon  Telephone No. 82-42-481-5605 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/KR02/02434

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☐ the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the claims:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, as amended (together with any statement) under Article 19  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheet \_\_\_\_\_

### 5.

- ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims	1 - 8	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 8	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 - 8	YES
	Claims		NO

**2. Citations and explanations (Rule 70.7)**

The following documents are referred to:

D1: WO-A-99/65892

D2: WO-A-2001/45484

**1. Novelty**

D1 and D2 disclose methods for preparing simvastatin of formula I, which is the final product of the present invention, with lovastatin as starting material. D1 is a method of directly introducing methyl group without hydrolyzing 8'-methylbutyryloxy group of lovastatin, which is different from the present invention in reaction mechanism. D2 is the same as the present invention in hydrolysis of 8'-methylbutyryloxy group with lactone ring, but is different from the present invention in that the present invention uses a mixed solvent of potassiumhydroxide-methanol-water as a base in hydrolysis step for producing triol acid of formula III, whereas D2 uses potassium t-butoxide.

Therefore, the subject matter of claims 1 to 8 seems to be novel (PCT Article 33(2)).

**2. Inventive Step**

For the analysis of the inventive step, D2 is considered the closest prior art. The preparation method of the present invention is different from that of D2 in that D2 relates to a method of preparing protected simvastatin by proceeding reaction by using potassium-t-butoxide in an organic solvent in hydrolysis of reaction step (i), and also using acyloxytriphenylphosphonium salt with a base in acylation step of reaction step (iii), whereas the present invention relates to a method for preparing protected simvastatin by using a mixed solvent of potassiumhydroxide-methanol-water in hydrolysis corresponding to the reaction step (i) of D2 and also using a quaternary ammonium halide or a quaternary phosphonium halide, a catalyst, in acylation reaction.

(Continued on Supplemental Sheet.)

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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## Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

Box V

Though both the present invention and the invention of D2 are of the same in the reaction material, intermediate, reaction step, but are different from each other in the catalyst used in each reaction step. Such a difference results in the present invention having no problem of D1: using potassium-t-butoxide, an expensive reagent. In addition, this difference gives the present invention an effect that it does not need to remove triphenylphosphine and unreacted 2,2-dimethylbutanoic acid, which are byproducts of acylation step. Further, such constitution of the present invention cannot be easily invented by a person skilled in the art by using the teaching of D2.

Therefore, the subject matter of claims 1 to 8 does involve an inventive step in the sense of PCT Article 33(3).

### 3. Industrial Applicability

Claims 1 to 8 meet the criteria set out PCT Article 33(4).